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10/716,825	11/18/2003	Gregory Stephanopoulos	MIN-P01-042	7074

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STEELE, AMBER D	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/716,825	STEPHANOPOULOS ET AL.	
	Examiner	Art Unit	
	AMBER D. STEELE	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 13, 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10 and 12-28* is/are pending in the application.

4a) Of the above claim(s) *2-4 and 12-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Please note: all cited references were provided previously with other Office actions.

Status of the Claims

1. The amendment received on October 2, 2006 canceled claim 7.

The amendment to the claims received on September 20, 2007 amended claims 1, 8, and 9 and canceled claim 11.

The amendment to the claims received on May 30, 2008 and entered on August 11, 2008 amended claims 1 and 8, canceled claims 7, 9, and 29-32, and added new claims 33-37.

The amendment to the claims received on February 13, 2009 amended claims 1 and 6 and canceled claims 8 and 33-37.

Claims 1-6, 10, and 12-28 are currently pending.

Claims 1, 5-6, and 10 are currently under consideration.

Election/Restrictions

2. Applicants elected, with traverse, Group I (previous claims 1-11) in the reply filed on October 2, 2006. Claims 12-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

3. Applicants elected, without traverse, mRNA as the species of expression level in the reply filed on October 6, 2006. Claims 2-4 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Priority

4. The present application (10/716,825, filed November 18, 2003) claims status as a CIP of U.S. application 10/060,048 filed January 29, 2002 and claims benefit of U.S. provisional application 60/427,265 filed November 18, 2002.

5. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, provisional Application No. 60/427,265, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. U.S. provisional application 60/427,265 does not teach the genes of Table 1.

However, this does not change the priority date of the claims. The claims presently have a priority date of January 29, 2002.

Invention as Claimed

6. A method for diagnosing an oral cancer in a patient comprising: (a) obtaining a biological sample from a patient, (b) determining the expression level of a plurality of genes associated with an oral cancer in the biological sample, thereby producing a test expression profile wherein the plurality of genes have GenBank™ Accession Nos. found in Table 1 (see claim 1 for list),

and (c) comparing the test expression profile with at least one signature expression profile from a patient known to have an oral cancer wherein said signature expression profile consists said plurality of genes and is indicative of an oral cancer wherein if the test expression profile substantially matches said signature expression profile the patient has the oral cancer and variations thereof.

Sequence Compliance

7. Applicants must either comply with the Sequence Rules (see the Office action mailed on November 28, 2007; section 7) or utilize the gene name in the claims. The examiner of record has not provided a Notice to Comply with the present Office action. However, if the accession numbers are present in the reply to the present Office action, a Notice to Comply will be mailed.

Withdrawn Rejections

8. The rejection of claims 1, 5-6, 8, 10, and 33-37 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter) is withdrawn in view of the claim amendments received on February 13, 2009 and in view of the specific support provided by applicants in the originally filed specification (see page 8 of the response received on February 13, 2009).

9. The rejection of claims 1, 5-6, 8, 10, and 33-37 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the claim amendments received on February 13, 2009.

Maintained Rejection

Claim Rejections - 35 USC § 112

10. Claims 1, 5-6, and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a **scope of enablement** rejection.

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue". These factors include, but are not limited to:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The level of skill in the art;
5. The level of predictability in the art;
6. The amount of direction provided by the inventor;
7. The presence or absence of working examples;
8. The quantity of experimentation necessary needed to make or use the invention based on the disclosure.

See *In re Wands* USPQ 2d 1400 (CAFC 1988):

The breadth of the claims and the nature of the invention:

The presently claimed invention is drawn to a method for diagnosing an oral cancer in a patient comprising: (a) obtaining a biological sample, (b) determining the expression level of a plurality of genes associated with an oral cancer in the biological sample, thereby producing a test expression profile wherein the plurality of genes have accession numbers (see 45 accession numbers recited in present claim 1), and (c) comparing the test expression profile with at least one signature expression profile of the plurality of genes is indicative of an oral cancer and variations thereof. Therefore, the presently claimed invention does not specify the minimum number or genes or the specific subset of genes necessary for diagnosis. In addition, the limitations of biological sample and oral cancer encompass broad genuses. The present claims do not provide any structural limitations regarding the genes in the test expression profile or signature expression profile and do not provide any structural information regarding the genes indicated by the 45 accession numbers. Accession numbers are fluid in nature and are constantly being updated wherein sequences are added, deletion, or altered. Thus, the accession numbers are associated with multiple sequences (i.e. entire gene sequence, fragments of the gene sequence, all sequences associated with the accession number, all ESTs, etc.). Accordingly, the claims encompass all known and unknown sequences currently associated with the accession number or those that will be associated with the accession number in the future and all known and unknown expression profiles (i.e. test and signature) and multiple sequences based on the association of multiple sequences with accession numbers (i.e. entire gene sequence, fragments of the gene sequence, all sequences associated with the accession number, all ESTs, etc.).

While the presently claimed method is enabled for screening biological samples for gene expression, the intended use as a means for diagnosing oral cancer is not enabled. The present

specification merely states that of the various genes were analyzed via GeneChip® array, the samples from five oral cancer patients (type, stage, etc. not specified) varied in 45 genes wherein 30 genes were "downregulated" and 15 of genes were "upregualted" (please refer to pages 69 and 72-73). The specification does not provide information regarding the level of upregualtion or downregulation compared to control (e.g. normal, noncancerous sample; statistically significant differences?; etc.). Accordingly, the claim scope is unduly broad with respect to encompassed genes and expression profiles.

The state of the prior art and the level of predictability in the art:

Diagnosis of oral cancer via altered gene expression is highly unpredictable, particularly in humans. Rosas et al. (Cancer Research 61: 939-942, 2001) teach that gene expression levels may not be altered, but rather methylation of the genes and only 23-56% of patients with head and neck primary tumors had hypermethylated genes (e.g. levels not conclusive for diagnostic purposes; please refer to abstract, Results, and Discussion sections). Liao et al. (Oral Oncology 36: 272-276, 2000) teach that 62.5% of patients with oral squamous cell carcinoma were positive for p53 mutations while 18.52% of samples from healthy patients had p53 mutations (e.g. not conclusive for diagnostic purposes; please refer to abstract and Discussion section). Furthermore, Williams (Journal of Clinical Pathology 53: 165-172, 2000) teach that oral squamous carcinogenesis is a multistep process involving multiple genetic events wherein not all genetic events occur in all squamous oral carcinogenesis or similar genetic alteration may occur at different times (please refer to abstract and Conclusion section). In addition, Scully et al., 2000, Genetic aberrations in oral or head and neck squamous cell carcinoma 3: clinico-pathological applications, Oral Oncology, 36: 404-413 teach that suspected markers are not always predictive

(i.e. diagnostic) including p53 and microsatellite instability at chromosomes 3p, 6p, 7q, 9p, 11p, and 11q (please refer to section 5.1). Furthermore, Schwartz, 2000, Biomarkers and Molecular Epidemiology and Chemoprevention of Oral Carcinogenesis, Crit. Rev. Oral Biol. Med, 1191): 92-122 teach that potential biomarkers must go through rigorous experimentation in order to have confidence in the ability of the biomarker(s) to define relative risk including animal model studies, expression of the marker in a staged transformation assay, expression of the marker in early pre-malignant human biopsies from a high risk group, and utilizing a large clinical population (see section III particularly subsection B). Moreover, Alevizos et al., 2001, Oral cancer in vivo gene expression profiling assisted by laser capture microdissection and microarray analysis, Oncogene, 20: 6196-6204 found 39 genes that were changed in 5 of 5 cases associated with oral cancer wherein some of the genes are not associated with present SEQ ID NOs: 1-43 (D86983 for example) and all 43 of the presently claimed genes are not associated with oral cancer (see Table 1). Additionally, Alevizos et al. discuss the differences between their results and two other studies (Shillitoe et al. and Leethanakul et al.) and suggest that the differences are reflective of different experimental approaches and methods of analysis (see pages 6200-6201). Hwang et al., 2003, Genomic dissection for characterization of cancerous oral epithelium tissues using transcription profiling, Oral Oncology, 39: 259-268 (provided by applicants in the IDS; NPL of present invention) teach that a large sampling size should be performed to validate the credibility of the identified discriminatory genes (i.e. the sample size presently utilized is not large enough to allow for statistically significant subclassification according to clinical characterization; n of 5), and suggests examining the effect of each factor on disease phenotype to fully understand the role of the gene in disease (see page 267).

Aris et al., 2004, Noise filtering and nonparametric analysis of microarray data underscores discriminating markers of oral, prostate, lung, ovarian, and breast cancer, BMC Bioinformatics, 5: 185-193 teach the potential issues of relying on Affymetrix GeneChip™ data for determining diagnostic markers for oral cancer including false positives (e.g. absence of error modeling 1,730 genes identified in oral cancer, with error modeling 129 genes identified in oral cancer; please refer to the abstract; Cancer-specific Biomarkers section). Hwang et al., 2002, Determination of minimum sample size and discriminatory expression patterns in microarray data, Bioinformatics, 18(9): 1184-1193 teach the importance of determining a minimum sample size when analyzing microarray data to determine statistical reliability (see abstract; pages 1189, 1191-1193). Stephanopoulos et al., 2002, Mapping physiological states from microarray expression measurements, Bioinformatics, 18(8): 1054-1063 teach that application of different classification methods may point to different genes, therefore, it is important especially for making conclusions regarding sample diagnosis to utilize multiple methods (see abstract; page 1062).

Therefore, the level of predictability in the art is dependent on many factors including data interpretation, statistical analysis, animal models (e.g. wherein animal knockouts could provide more definitive evidence), long-term studies (e.g. following patients throughout course of disease to determine if gene expression is altered), etc. While finding genetic markers to accurately diagnose oral cancer is important, the state of the art requires vast amounts of data including correlation of the gene to cancer with high probability, potentially finding one or more genetic markers for each oral cancer, detailed statistical analysis of data, etc. In addition, a

showing that the genetic markers are specific for oral cancer and modulation is not associated with other diseases is required.

The level of skill in the art:

The level of skill would be high, most likely at the Ph.D. level.

The amount of direction provided by the inventor and the existence of working examples:

There are no specific examples directed to the intended use language of the presently claimed invention (i.e. diagnosing oral cancer in patients), nor is there any information provided regarding correlating the altered gene expression data provided in the specification and diagnosing oral cancer. The specification contains only cursory statements that various genes are "down" or "up" in cancer (please refer to Table 1).

The quantity of experimentation needed to make or use the invention based on the content of the disclosure:

In light of the unpredictability surrounding the claimed subject matter, the undue breadth of the claimed invention's intended use, and the lack of adequate guidance, one wishing to practice the presently claimed invention would be unable to do so without engaging in undue experimentation. One wishing to practice the presently claimed invention would have to facilitate clinical studies with large numbers of patients suffering from each known oral cancer and screen the entire genome to determine if any genes may be correlated to cancer, determine which sequences are relevant to the genes of the recited accession numbers, follow patients for years to determine if gene expression changes during the course of cancer, provide detailed statistical analysis of the data to limit potential false positives/negatives, etc.

Arguments and Response

11. Applicants' arguments directed to the rejection under 35 USC 112, first paragraph (scope of enablement), for claims 1, 5-6, and 10 were considered but are not persuasive for the following reasons.

Applicants contend that the claim amendments obviate the rejection. In addition, applicants contend that the present specification provides working examples to show that all the 45 genes are differentially expressed in oral cancer patients and that one of skill in the art would know that the expression profile could be utilized to successfully diagnose oral cancer. Applicants also contend that the present specification teaches how to measure gene expression levels in a biological sample and how to compare the test expression profile with a signature expression profile. Applicants also contend that the level of skill in the art was high at the time of filing and all of the techniques were known in the art and highly reliable. Furthermore, applicants contend that the examiner of record has not provided adequate reasoning to support the contention that the claims are not enabled for a method of diagnosing oral cancer and contend that the cited references are irrelevant because the references do not relate to all 45 genes in present claim 1.

Applicants' arguments are not convincing because the claim amendments do not negate the scope of enablement rejection. The present rejection is a scope of enablement rejection, therefore, the enablement of screening for differences in gene expression between samples is not in contention. However, the intended use as a method for diagnosing an oral cancer in a patient is not enabled. Pages 69-80 of the present specification caution that diagnosis requires (1) determining which genes are relevant to disease and (2) determining a gene pattern that is a

marker of a physiological state, but also questions whether the patterns can be utilized to diagnose cells or tissue samples (please refer to the paragraph spanning pages 69-70). In addition, it is noted that applicants have tested a very small number of samples (i.e. five patients) in determining that the accession numbers are "diagnostic". In addition, the present specification utilized patients known to have oral cancer. Thus, no working examples are present which actually diagnose patients with oral cancer (e.g. utilizing "normal" samples, utilizing samples from patients that were not previously diagnoses with oral cancer, etc.; see page 69 of the present specification). While techniques for expression profiling (i.e. screening for gene expression) are well known in the art, specific genetic markers to diagnose oral cancer are not well known in the art. Thus, applicants are enabled for screening for gene expression, but have not provided an enabling disclosure for diagnosing oral cancer.

Diagnosis of oral cancer via altered gene expression is highly unpredictable, particularly in humans. See the references cited in the rejection above. Therefore, despite applicants' contention that the examiner of record has only provided irrelevant references in the rejection, it is the examiner's position that the references are relevant in that the references pertain to the difficulties in determining genetic markers for oral cancer and the difficulties in analyzing expression profiles from microarray data (e.g. false negatives, false positives, etc.). In addition, the arguments of counsel cannot take the place of evidence in the record. See *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965) and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). See MPEP § 2145 and § 716.01(c).

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1, 5-6, and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 USC 112, first paragraph "Written Description" requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a **written description** rejection.

Claim 1 is drawn to a method for diagnosing an oral cancer in a patient comprising (a) obtaining a biological sample from a patient, (b) determining the expression level of a plurality of genes associated with oral cancer (see claimed accession numbers), and (c) comparing the test expression profile with at least one signature expression profile of the plurality of genes. The invention as claimed encompasses all known sequences associated with the accession numbers, all genes which may potentially be associated with the accession numbers in the future, and any yet to be discovered sequences associated with the accession numbers. In addition, any type of oral cancer is included in the claimed method. The claimed invention does not include any structural information regarding the accession numbers.

The specification teaches 45 genes (please refer to Table 1). In addition, the specification teaches that of the various genes analyzed utilizing the GeneChip® array only 30 of the genes were "downregulated" and 15 of the genes were "upregualted" in five patients with oral cancer wherein the specific type of oral cancer is not disclosed (please refer to pages 69 and 72-73). However, the claimed invention does not include any structural limitations regarding the accession numbers. Accession numbers are fluid in nature and are constantly being updated and altered. Thus, one of skill in the art would not determine that applicants had possession of every sequence associated with every accession number and the ability to diagnose every type of oral cancer. Further exacerbating the lack of written description is the lack of an association between some of the accession numbers with any sequences or the association of the gene name with multiple sequences (i.e. HG3549-HT3751 and Wilm Tumor-Related Protein; HG2992-HT5186 and Beta-Hexosaminidase, Alpha; please refer to the NCBI printouts provided in the application history on November 28, 2007). Furthermore, the claimed invention does not teach how the genes can be utilized to diagnose oral disease (e.g. correlation of gene expression to disease; level of upregulation or downregulation expected in diseased samples, etc.). Therefore, one skilled in the relevant art would not reasonably conclude that the Applicants had possession of the invention as claimed since the structural limitations of the accession numbers are not included in the claimed invention and diagnosis of oral cancer via the accession numbers has not been established.

See Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was *in possession of the invention.* The invention is, for purposes of the 'written description'

inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.).

With the exception of analyzing an oral cancer sample for expression of the 45 genes (i.e. not every sequence associated with each accession number) as disclosed by the specification, the skilled artisan cannot envision the method of claim 1. In addition, it is noted that while the art recognizes certain genetic markers that may correlate to oral diseases a specific, definitive genetic marker for diagnosing oral diseases including oral cancer have not been recognized in the art. For example, (1) Rosas et al. (Cancer Research 61: 939-942, 2001; provided previously) teach that gene expression levels may not be altered, but rather methylation of the genes may be altered in head and neck tumors (i.e. only 23-56% of patients with head and neck primary tumors had hypermethylated genes; e.g. levels not conclusive for diagnostic purposes; please refer to abstract, Results, and Discussion sections), (2) Liao et al. (Oral Oncology 36: 272-276, 2000; provided previously) teach that 62.5% of patients with oral squamous cell carcinoma were positive for p53 mutations while 18.52% of samples from healthy patients had p53 mutations (e.g. not conclusive for diagnostic purposes; please refer to abstract and Discussion section), and (3) Williams (Journal of Clinical Pathology 53: 165-172, 2000; provided previously) teach that oral squamous carcinogenesis is a multistep process involving multiple genetic events wherein not all genetic events occur in all squamous oral carcinogenesis or similar genetic alteration may occur at different times (please refer to abstract and Conclusion section). Thus, while the art recognizes genetic markers that may correlate to oral diseases (e.g. associated with an oral disease or determining if a patient has a higher risk of having an oral disease), the art does not

presently recognize one or more genetic markers that can be utilized to definitively diagnose oral diseases including oral cancer. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class wherein the specification provided only the bovine sequence.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1, 5-6, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Independent claim 1 refers to various genes by GenBank™ accession number. Since accession numbers are affiliated with various sequences, it is not clear if the accession numbers require a specific sequence, the entire gene sequence, a sequence associated with the accession number, an EST, etc. In addition, the database is constantly being updated. Therefore, the sequences associated with the accession numbers change over time.

16. Claim 1 contains the trademark/trade name GenBank™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or

trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a database comprising sequences and, accordingly, the identification/description is indefinite.

17. Claims 1, 5-6, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. For example, it is not clear if all 45 accession numbers are required in the test expression profile or if only a subset, etc. of accession numbers are required in the test expression profile. In addition, it is not clear if all 45 accession numbers are required in the signature expression profile or if only a subset, etc. of accession numbers are required in the signature expression profile.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

19. Claims 1, 5-6, and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Katz et al. U.S. Patent 6,797,471 filing date of August 6, 2001 and effective filing date of August 4, 2000.

For present claim 1, Katz et al. teach methods of identifying a subject at risk for developing smoking related cancers including obtaining a biological sample, determining expression levels of genes, and comparing to controls (e.g. signature expression profile; please refer to the entire specification particularly abstract; Figures 1-2 and 10-12; columns 3-6 and 8-21; claims 1-21). In addition Katz et al. teach utilizing genes from chromosomes 2, 3 (specifically 3p21.3), 5, 9, 10 (specifically 10q22), 17, 18, and 22 (i.e. genes of Table 1 associated with chromosomes 2, 3, 5, 9, 10, 17, 18, and 22 including fiberblast growth factor 8, KIAA0089, urokinase plaminogen activator, deoxyribonuclease 1-like 3, cytochrome P4502C9 subfamily IIC, diazepam binding inhibitor, cytochrome C oxidase subunit Vb, IL-8Rβ, transcription factor 20, KIAA-172, cathepsin L, aldehyde dehydrogenase 10, and lysophospholipase like; please refer to the entire specification particularly the abstract, column 1, lines 56-67; column 2, lines 1-57; column 8, lines 56-67).

For present claim 5, Katz et al. teach determining mRNA expression (please refer to the entire specification particularly column 16, lines 32-40; column 18, lines 35-54).

For present claim 6, Katz et al. teach isolating nucleic acids from the samples (please refer to the entire specification particularly column 14, lines 66-67; column 15, lines 1-4).

For present claim 10, Katz et al. teach biological samples including tissue and fine needle aspirations (please refer to the entire specification particularly column 3, lines 21-28; column 14).

Therefore, the presently claimed invention is anticipated by the teachings of Katz et al.

20. Claims 1, 5-6, and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Warrington et al. U.S. Patent 7,108,969 filing date of September 10, 2001 and effective filing date of September 8, 2000.

For present claim 1, Warrington et al. teach methods for monitoring gene expression profiles associated with oral cancer comprising obtaining a biological sample, determining, determining expression levels of genes, and comparing to controls (e.g. signature expression profile; please refer to the entire specification particularly abstract; Figures 1A, 1B, 2A, 2B, 2C, 3-6, 7A-7K; columns 2-13; Examples I-IV; claims 1-19). In addition, Warrington et al. teach accession numbers X76029, U34252, M69177, X02419, X78932, U46689, Y09616, M57731, Z29083, U18934, J04469, M11147, D13643, M61855, U67963, X07695, D43968, D42047, M34309, M14200, S45630, U56814, X87241, D79994, M30818, U06643, U24577, X15183, and X12451 among others (i.e. genes of Table 1; please refer to Figures 2A, 2B, 2C, 2D, 3, 6, 7A-7K).

For present claim 5, Warrington et al. teach determining mRNA expression (please refer to the entire specification particularly column 6, lines 31-54; column 7, lines 29-43; Example II).

For present claim 6, Warrington et al. teach isolation of nucleic acids from samples (please refer to the entire specification particularly column 7, lines 29-43; Example I).

For present claim 10, Warrington et al. teach biological samples including tissue, blood (e.g. serum), and fine needle biopsy (e.g. aspirates; please refer to the entire specification particularly column 7, lines 29-57).

Therefore, the presently claimed invention is anticipated by the teachings of Warrington et al.

Conclusion

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1639

April 29, 2009